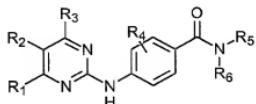


What is claimed is:

1. A method for treating a condition responsive to inhibition of the JNK pathway, comprising administering to a patient in need thereof and effective amount of a compound having the structure:



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or a pharmaceutically acceptable salt thereof,

wherein:

R₁ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R₇;

R₂ and R₃ are the same or different and are independently hydrogen or lower alkyl;

R₄ represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉, -(CH₂)_aC(=O)NR₉(CH₂)_bC(=O)R₁₀, -(CH₂)_aNR₉C(=O)R₁₀, -(CH₂)_aNR₁₁C(=O)OR₉, -(CH₂)_aNR₉R₁₀, -(CH₂)_aOR₉, -(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR₉R₁₀;

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or R₅ and R₆ taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉, -C(=O)NR₉OR₈, -SO_cR₈, -SO_cNR₈R₉, -NR₈SO_cR₉, -NR₈R₉, -NR₈C(=O)R₉, -NR₈C(=O)(CH₂)_bOR₉, -NR₈C(=O)(CH₂)_bR₉, -O(CH₂)_bNR₈R₉, or heterocycle fused to phenyl;

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R₈, R₉, R₁₀ and R₁₁ are the same or different and at each occurrence

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independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;
or R₈ and R₉ taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;
a and b are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and
c is at each occurrence 0, 1 or 2.

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2. The method of claim 1 wherein the condition is an inflammatory or autoimmune condition.

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3. The method of claim 2 wherein the inflammatory or autoimmune condition is rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis, Crohn's disease, gastritis, esophagitis, hepatitis, pancreatitis, nephritis, psoriasis, eczema, dermatitis, multiple sclerosis, Lou Gehrig's disease, sepsis, conjunctivitis, acute respiratory distress syndrome, purpura, nasal polip or lupus erythematosus.

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4. The method of claim 1 wherein the condition is a cardiovascular, metabolic or ischemic condition.

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5. The method of claim 4 wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infarction, ischemic diseases of heart, kidney, liver, and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

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6. The method of claim 1 wherein the condition is an infectious disease.

7. The method of claim 6 wherein the infectious disease is a viral infection.

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8. The method of claim 7 wherein the viral infection is caused by human

immunodeficiency virus, hepatitis B virus, hepatitis C virus, human papilomavirus, human T-cell leukemia virus or Epstein-Barr virus.

9. The method of claim 1 wherein the condition is cancer.

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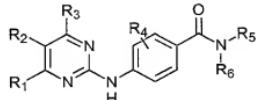
10. The method of claim 9 wherein the cancer is of the colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, testes, urinary bladder, ovary or uterus.

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11. The method of claim 1 wherein the condition is stroke, epilepsy, Alzheimer's disease or Parkinson's disease.

12. The method of claim 9 further comprising administering an effective amount of a cytotoxic agent or radiation therapy.

15 13. A method for treating an inflammatory or an autoimmune condition comprising administering to a patient in need thereof an effective amount of a compound having the structure:



20 or a pharmaceutically acceptable salt thereof,

25 wherein:

R₁ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R₇;

R₂ and R₃ are the same or different and are independently hydrogen or lower alkyl;

30 R₄ represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉, -(CH₂)_aC(=O)NR₉R₁₀, -(CH₂)_aNR₉C(=O)R₁₀, -(CH₂)_aNR₉(CH₂)_bC(=O)R₁₀,

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-(CH₂)_aNR₁₁C(=O)NR₉R₁₀, -(CH₂)_aNR₉R₁₀, -(CH₂)_aOR₉,
 -(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR₉R₁₀;
 or R₅ and R₆ taken together with the nitrogen atom to which they are
 attached to form a heterocycle or substituted heterocycle;
 R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro,
 carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl,
 sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted
 aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl,
 substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉,
 -C(=O)NR₈OR₉, -SO_cNR₈R₉, -NR₈SO_cR₉, -NR₈R₉, -
 NR₈C(=O)R₉, -NR₈C(=O)(CH₂)_bOR₉, -NR₈C(=O)(CH₂)_bR₉,
 -O(CH₂)_bNR₈R₉, or heterocycle fused to phenyl;
 R₈, R₉, R₁₀ and R₁₁ are the same or different and at each occurrence
 independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl,
 aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle,
 heterocyclealkyl or substituted heterocyclealkyl;
 or R₈ and R₉ taken together with the atom or atoms to which they are
 attached to form a heterocycle or substituted heterocycle;
 a and b are the same or different and at each occurrence independently
 selected from 0, 1, 2, 3 or 4; and
 c is at each occurrence 0, 1 or 2.

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14. The method of claim 13 further comprising administering an effective amount of an anti-inflammatory agent.

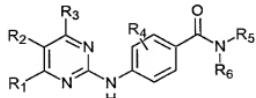
15. The method of claim 14, wherein the anti-inflammatory agent is

salicylic acid, acetylsalicylic acid, methyl salicylate, diflunisal, salsalate, olsalazine, sulfasalazine, acetaminophen, indomethacin, sulindac, etodolac, mefenamic acid, meclofenamate sodium, tolmetin, ketorolac, dichlofenac, ibuprofen, naproxen, naproxen sodium, fenoprofen, ketoprofen, flurbiprofen, oxaprozin, piroxicam, meloxicam, ampiroxicam, droxicam, pivoxicam, tenoxicam, nabumetome, phenylbutazone, oxyphenbutazone, antipyrine, aminopyrine, apazone and nimesulide, zileuton, aurothioglucose, gold sodium thiomolate, auranofin, colchicine, allopurinol, probenecid, sulfapyrazone, benz bromarone, enbrel, infliximab, anakinra, celecoxib or rofecoxib.

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16. The method of claim 13, wherein the inflammatory or autoimmune condition is rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis, 5 Crohn's disease, gastritis, esophagitis, hepatitis, pancreatitis, nephritis, psoriasis, eczema, dermatitis, multiple sclerosis, Lou Gehrig's disease, sepsis, conjunctivitis, acute respiratory distress syndrome, purpura, nasal polip or lupus erythematosus.

17. A method for treating a cardiovascular, metabolic or ischemic 10 condition comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R₁ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R₇;

R₂ and R₃ are the same or different and are independently hydrogen or lower alkyl;

R₄ represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, 25 hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉,

-(CH₂)_aC(=O)NR₉(CH₂)_bC(=O)R₁₀, -(CH₂)_aNR₉C(=O)R₁₀,

-(CH₂)_aNR₁₁C(=O)NR₉R₁₀, -(CH₂)_aNR₉R₁₀, -(CH₂)_aOR₉,

-(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR₉R₁₀;

or R₅ and R₆ taken together with the nitrogen atom to which they are 30 attached to form a heterocycle or substituted heterocycle;

R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl,

sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted

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aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉, -C(=O)NR₈OR₉, -SO_cR₈, -SO_cNR₈R₉, -NR₈SO_cR₉, -NR₈R₉, -NR₈C(=O)R₉, -NR₈C(=O)(CH₂)_bOR₉, -NR₈C(=O)(CH₂)_bR₉, -O(CH₂)_bNR₈R₉, or heterocycle fused to phenyl;

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R₈, R₉, R₁₀ and R₁₁ are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R₈ and R₉ taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

a and *b* are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.

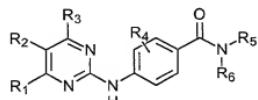
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18. The method of claim 17, wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infarction, ischemic diseases of heart, kidney, liver, and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

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19. A method for treating an infectious disease comprising administering to a patient in need thereof an effective amount of a compound having the structure:

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or a pharmaceutically acceptable salt thereof,

wherein:

R₁ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R₇;

R₂ and R₃ are the same or different and are independently hydrogen or lower alkyl;

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R₄ represents one to four optional substituents, wherein each substituent is

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the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉, -(CH₂)_aC(=O)NR₉CH₂bC(=O)R₁₀, -(CH₂)_aNR₉C(=O)R₁₀, -(CH₂)_aNR₉C(=O)NR₉R₁₀, -(CH₂)_aNR₉R₁₀, -(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR_cR₁₀;

or R₅ and R₆ taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

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R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉, -C(=O)NR₈OR₉, -SO_cR₈, -SO_cNR₈R₉, -NR₈SO_cR₉, -NR₈R₉, -NR₈C(=O)R₉, -NR₈C(=O)(CH₂)_bOR₉, -NR₈C(=O)(CH₂)_bR₉, -O(CH₂)_bNR₈R₉, or heterocycle fused to phenyl;

R₈, R₉, R₁₀ and R₁₁ are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R₈ and R₉ taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

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a and b are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.

20. The method of claim 19 wherein the infectious disease is a viral infection.

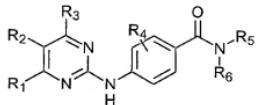
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21. The method of claim 20 wherein the viral infection is caused by human immunodeficiency virus, hepatitis B virus, hepatitis C virus, human papillomavirus, human T-cell leukemia virus or Epstein-Barr virus.

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22. A method for treating cancer comprising administering to a patient in

need thereof an effective amount of a compound having the structure:



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or a pharmaceutically acceptable salt thereof,

wherein:

10 R_1 is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R_7 ;

R_2 and R_3 are the same or different and are independently hydrogen or lower alkyl;

15 R_4 represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

20 R_5 and R_6 are the same or different and independently $-R_8$, $-(CH_2)_aC(=O)R_9$, $-(CH_2)_aC(=O)OR_9$, $-(CH_2)_aC(=O)NR_9R_{10}$, $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$, $-(CH_2)_aNR_9C(=O)NR_9R_{10}$, $-(CH_2)_aNR_9C(=O)OR_9$, $-(CH_2)_aSO_2R_9$, or $-(CH_2)_aSO_2NR_9R_{10}$;

or R_5 and R_6 taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

25 R_7 is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-OC(=O)R_8$, $-C(=O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_2R_8$, $-SO_2NR_8R_9$, $-NR_8SO_2R_9$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$, $-O(CH_2)_bNR_8R_9$, or heterocycle fused to phenyl;

30 R_8 , R_9 , R_{10} and R_{11} are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

35 or R_8 and R_9 taken together with the atom or atoms to which they are

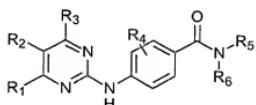
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attached to form a heterocycle or substituted heterocycle;
a and b are the same or different and at each occurrence independently
selected from 0, 1, 2, 3 or 4; and
c is at each occurrence 0, 1 or 2.

23. The method of claim 22 further comprising administering an effective amount of an anti-cancer agent.

24. The method of claim 23 wherein the anti-cancer agent is
10 cyclophosphamide, Ifosfamide, trofosfamide, Chlorambucil, carmustine (BCNU), Lomustine (CCNU), busulfan, Treosulfan, Dacarbazine, Cisplatin, carboplatin, vincristine, Vinblastine, Vindesine, Vinorelbine, paclitaxel, Docetaxol, etoposide, Teniposide, Topotecan, 9-aminocamptothecin, camptothecin, crizotinib, mytomycin C, methotrexate, Trimetrexate, mycophenolic acid, Tiazofurin, Ribavirin, EICAR, hydroxyurea, deferoxamine, 5-fluorouracil, Flouxuridine, Doxifluridine, Ratitrexed, cytarabine (ara C), cytosine arabinoside, fludarabine, mercaptopurine, thioguanine, Tamoxifen, Raloxifene, megestrol, goserelin, Leuprolide acetate, flutamide, bicalutamide, B 1089, CB 1093, KH 1060, verteporfin (BPD-MA), Phthalocyanine, photosensitizer Pc4, demethoxyhypocrellin A (2BA-2-DMHA), interferon- α , interferon- γ , tumor-necrosis factor, Lovastatin, 1-methyl-4-phenylpyridinium ion, staurosporine, Actinomycin D, Dactinomycin, bleomycin A2, Bleomycin B2, Peplomycin, daunorubicin, Doxorubicin (adriamycin), Idarubicin, Epirubicin, Pirarubicin, Zorubicin, Mitoxantrone, verapamil or thapsigargin.

25. The method of claim 22 wherein the cancer is of the colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, testes, urinary bladder, ovary or uterus.

26. A method for treating stroke, epilepsy, Alzheimer's disease, or Parkinson's disease comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R₁ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R₇;

R₂ and R₃ are the same or different and are independently hydrogen or lower alkyl;

R₄ represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉, -(CH₂)_aC(=O)NR₈(CH₂)_bC(=O)R₁₀, -(CH₂)_aNR₉C(=O)R₁₀, -(CH₂)_aNR₁₁C(=O)NR₉R₁₀, -(CH₂)_aNR₉R₁₀, -(CH₂)_aOR₉, -(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR₉R₁₀;

or R₅ and R₆ taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉, -C(=O)NR₈OR₉, -SO_cR₈, -SO_cNR₈R₉, -NR₉SO_cR₈, -NR₈R₉, -NR₈C(=O)R₉, -NR₈C(=O)(CH₂)_bOR₉, -NR₈C(=O)(CH₂)_bR₉, -O(CH₂)_bNR₈R₉, or heterocycle fused to phenyl;

R₈, R₉, R₁₀ and R₁₁ are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R₈ and R₉ taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

a and b are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.